

REPLACED BY  
ART 34 AMDT

## CLAIMS

1. Use of an embryonic marker to positively identify viable precursor cells that have entered a specific post-natal differentiation pathway, wherein the embryonic marker is an expressed morphogenic protein, a homolog thereof or a marker co-expressed and/or co-detectable with this marker.

2. Use of an embryonic marker to positively identify viable skeletal precursor cells that have entered a post-natal skeletal differentiation pathway, a homolog thereof or a marker co-expressed and/or co-detectable with this marker, whereby the positive marker is characterised by the absence of a negative marker.

3. The use according to claim 2, wherein the negative marker is FGFR3 or a marker or factor co-expressed or co-detectable with this negative marker.

4. The use according to any previous claim wherein the positive marker is a gene or a protein or an mRNA expressed by a gene in the precursor cells or a part thereof, detectable at the DNA, the RNA or the protein level and/or detectable via the activity of a promoter directing/regulating this gene expression, operably linked to a heterologous reporter gene.

5. The use according to any previous claim wherein the embryonic marker identifies precursor cells in skeletal development of mammals.

6. The use according to any previous claim wherein the embryonic marker identifies precursor cells belonging to a joint interzone in mammals.

7. The use according to any previous claim wherein the expressed morphogenic protein is the cartilage-derived morphogenic protein CDMP-1 or a transforming growth factor  $\beta$  having at least 80% homology with CDMP-1 as a marker of skeletal precursor cells from any part of the body or a marker or factor co-expressed or co-detectable with any or all of these positive markers.

8. Use of reagents, ligands, and/or antibodies recognizing cell surface markers for sorting and enriching of precursor cells, wherein the cell surface marker is co-expressed or co-detectable with the marker of any of claims 1 to 7.

9. Use of reagents, ligands, and/or antibodies recognizing cell surface markers according to claim 8, for sorting of skeletal precursor cells and for enriching a population in skeletal precursor cells.

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10. Use of enriching via cell sorting according to claims 8 or 9, wherein cell sorting methods comprise fluorescence activated cell sorting, the use of magnetic beads coated with the respective antibodies or ligands, the use of affinity chromatography or the use of any other means coated with antibodies or ligands directed to the cells which are to be selected.

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11. Use of reagents and/or antibodies according to any of claims 8 to 10 wherein the antibodies are polyclonal or monoclonal antibodies.

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12. Use of skeletal precursor cells marked according to any of claims 1 to 7 for producing or repairing connective tissue in a mammal.

13. Use according to claim 12, wherein the said cells are cultured at a cell density of at least  $10^5$  cells/ml.

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14. Use according to claim 12 or claim 13, comprising further administration of a factor that stimulates differentiation of the skeletal precursor cells into the type of connective tissue to be produced or repaired.

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15. Use of precursor cells marked according to any of claims 1 to 7 as a source of growth factors.

16. Use of precursor cells marked according to any of claims 1 to 7 as matrix producing cells.

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17. Use according to claim 16, wherein the said matrix further comprises a bio-resorbable polymer or carrier.

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18. Use according to claim 16 or 17 for the treatment of subglottic stenosis, tracheomalacia, chondromalacia patellae, osteoarthritis and traumatic lesions in a mammal.

19. A procedure for joint surface defect repair in a mammal comprising the co-implantation of skeletal precursor cells marked according to any of claims 2 to 7 and chondrocytes.

20. A method for enhancing the implantation of a prosthetic device in connective tissue comprising the step of implanting a prosthetic device having skeletal precursor cells according to any of the claims 1 to 7 adhered thereto under conditions suitable for differentiating the cells into the connective tissue desired.

21. A method of obtaining a culture of viable precursor cells having entered a specific post-natal differentiation pathway comprising the steps of:

applying a binding agent for an embryonic marker to a source of cells having the precursor cells, the marker positively identifying the viable precursor cells that have entered a specific post-natal differentiation pathway, wherein the embryonic marker is an expressed morphogenic protein, a homolog thereof or a marker co-expressed and/or co-detectable with this marker; and

separating the cells which are bound to the binding agent.

22. A method of obtaining a culture of viable skeletal precursor cells having entered a specific post-natal differentiation pathway comprising the steps of:

applying a binding agent for an embryonic marker to a source of cells having the precursor cells, wherein the marker positively identifies viable skeletal precursor cells that have entered a post-natal skeletal differentiation pathway, or is a homolog thereof or is a marker co-expressed and/or co-detectable with this positive marker, whereby the positive marker is characterised by the absence of a negative marker; and

separating the cells which are bound to the binding agent.

23. A culture of viable precursor cells that have entered a specific post-natal differentiation pathway, wherein cells express an embryonic marker which is an expressed morphogenic protein, a homolog thereof or a marker co-expressed and/or co-detectable with this marker.

24. A culture of viable skeletal precursor cells expressing an embryonic marker positively identifying the viable skeletal precursor cells that have entered a post-natal skeletal differentiation pathway, a homolog thereof or a marker co-expressed

and/or co-detectable with this marker, whereby the positive marker is characterised by the absence of a negative marker.

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25. A therapeutic composition comprising the cells of claim 23 or 24.
26. An implant comprising the cells of claim 23 or 24.
27. The implant of claim 26 suitable for connective tissue implantation.
- 10 28. A method of treating a patient in need thereof comprising administration of the therapeutic composition of claim 25.
- 15 29. A diagnostic for identifying a positive marker of viable precursor cells, wherein the marker is an expressed morphogenic protein, a homolog thereof or a marker co-expressed and/or co-detectable with this marker.
- 20 30. A diagnostic for identifying viable skeletal precursor cells that have entered a post-natal skeletal differentiation pathway, a homolog thereof or a marker co-expressed and/or co-detectable with this marker, whereby diagnostic also identifies the absence of a negative marker.